

GENERAL PARALYSIS OF THE INSANE *†

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Give me the power to produce fever, and I will cure all disease.—HIPPOCRATES.

Introduction

Although the origin of syphilis is still disputed, there is general agreement that the first appearance of the disease in epidemic proportion in Europe occurred during the campaign in Italy undertaken by Charles VIII of France at the end of the 15th century. This was a total failure and ended in a disorganized retreat of his armies, who scattered over Europe and left a trail of disease which was contagious, mutilating, and venereal. The Italians called it the "French disease", but the French preferred to name it "Neapolitan".

To British psychiatry belongs the credit of the first clinical description of general paralysis of the insane (GPI) as a separate entity. John Haslam (1798), surgeon-apothecary to Bethlem, wrote an account of a man aged 42, who was admitted in June, 1795, and died in August, 1796, in which he gave a description of the classical grandiose type.‡

At the beginning of the 19th century the French school—of whom Bayle (1826) was one of the chief exponents—continued clinical researches on GPI, and Esquirol (1838), the first physician to give a course of lectures on mental diseases, referred not only to the fatal issue of GPI, but also to its more frequent incidence in the male.

In Great Britain little progress was made and the position of GPI was ill-defined: Prichard of Bristol in a treatise on insanity (1835) was largely influenced by the French writers of the same time, and he came to the conclusion that GPI was a rare disease in Great Britain compared to the higher prevalence in the Paris hospitals.

In 1883 Sir Thomas Clouston emphasized the entity of GPI but did not think there was any proof that it was syphilitic in origin. Mickle, the medical superintendent of Grove Hall Asylum, London, published an extensive treatise on GPI in 1880, and a much enlarged and revised edition

appeared 6 years later. He records that "military and naval life, occupations exposing the workers to great heat and sweat, or to alternate heat and cold draughts, and prostitution—all favour the production of general paralysis". He continues:

Of the soldiers admitted under my care during a number of years, 18 per cent. were general paralytics. I found the regiment of the Guards, the flower of the Army, yield the highest ratio of general paralysis in the total number coming under care of unsound mind. In soldiers there are several factors: among the officers the tension of anxious responsibility; among all grades the violent emotions and privations of war, the shock of artillery discharge, of bursting shells; but, especially, alcoholic and sexual excess and venereal disease.

At that time nearly 13 per cent. of all male admissions to mental hospitals were suffering from GPI. Treatment was entirely palliative, and eventually removal to an asylum was recommended. In the prodromal stages of the disease we are exhorted to exercise "tact and gentleness. Every source of mental worry, anxiety, annoyance, fear, chagrin, should be scrupulously avoided at almost any cost. All intellectual labour should cease, and just such an amount of reading, of conversation, and of thought, should be undertaken as will afford the most gentle of intellectual and emotional exercise". However, if the differential diagnosis between cerebral syphilis, which was then recognized, and GPI was uncertain, a short course of mercurials followed by a longer course of iodides was enjoined.

In 1895 Sir Frederick Mott, whose work prepared the ground for the final solution, was appointed Director of the Central Laboratory and Pathologist to the London County Asylums at Claybury. He was undoubtedly influenced by Fournier's conception of parasyphilis and his description of congenital syphilis. In the first volume of the *Archives of Neurology*, published in 1900, Mott wrote:

It is no argument against syphilis being the cause of those affections which are termed parasyphilitic, to say that because iodide of potassium and mercury do no good the diseases are, therefore, not of syphilitic origin. We might as well expect by giving such drugs to be able to give new teeth or to convert a dwarf into a full-sized man.

His theory of the syphilitic origin of the disease

* Received for publication, October 28, 1955.

† Presidential Address to Section of Psychiatry, Royal Society of Medicine, delivered on October 11, 1955.

‡ D. Leigh (*J. Hist. Med.*, 10, 1) queries the belief that Haslam actually described general paralysis as a clinical entity. He describes the appearances of the brain in 37 autopsies performed at Bethlem, but only Case 15 might be considered to be general paralysis.

was re-inforced by the study and history of cases of juvenile GPI which he had collected.

In 1905 Schaudinn and Hoffman demonstrated the causal agent of syphilis as a small spiral organism known as the *Spirochaeta pallidum*. August von Wassermann in 1906 discovered that in the blood of patients suffering from syphilis were changes detectable by laboratory methods—by this means it became possible to detect victims of syphilis, even when the disease was quiescent and the patient symptomless. Felix Plaut in 1907 carried Wassermann's researches still further to the examination of the cerebrospinal fluid. In 1913 Hideyo Noguchi demonstrated the presence of spirochaetes in the brain of a patient who had died of general paralysis and so, 115 years after Haslam's clinical description of the disease, conclusive proof was obtained that GPI is an organic disease of the brain caused by syphilis.

Chemotherapy

For over 400 years mercury was the only therapeutically active preparation employed: there was no real advance in the treatment of syphilis until the 20th century. The first step forward was the introduction of an arsenical compound—Salvarsan (606)—by Ehrlich in 1910. Unfortunately, the trivalent form, in which arsenic was originally introduced, was of no value in the treatment of GPI. Mott (1915) offered little hope of the cure of GPI, the fatal outcome of which had long been recognized:

I have come to the conclusion that those late degenerative forms of syphilis of the nervous system (and I refer especially to general paralysis), have not been cured, nor even greatly benefited, by any treatment with salvarsan or neosalvarsan, whether administered intravenously or intrathecally.

We must rather look to the prevention of the spread of syphilis, and its early diagnosis and treatment by modern methods, as the most hopeful way of combating this terrible malady.

In the meantime various workers demonstrated that inadequate treatment had the disadvantage of shortening the interval between infection and the appearance of symptomatic neurosyphilis, as compared with cases which were untreated. It was not until 1919, when Jacobs and Heidelberger synthesized a pentavalent arsenical, tryparsamide, that there was any real advance in the chemotherapy of GPI. This preparation, in contrast to the trivalent compounds, was relatively useless in early and somatic syphilis, but it was of considerable value in the treatment of GPI and late neurosyphilis. Sézary and Barbé, as quoted by Dattner (1944), suggested that the action of the pentavalent arsenicals depended upon reduction processes, whereas the trivalent drugs required oxidation to activate them. This hypothesis would serve to explain their con-

trary therapeutic activities since brain tissue has no oxidizing properties. In Great Britain, Hawking and others (1937) found that the intravenous injection of 3 g. of tryparsamide produced treponemacidal activity in the spinal fluid, whereas the comparable administration of trivalent compounds was without effect. The first report of the use of tryparsamide in the treatment of GPI came from Lorenz, Loevenhart, Bleckwenn, and Hodges in 1923, since when it has been extensively employed. It was found that general paralytics improved physically and remissions were obtained in about 30 per cent. of cases. But it had one great disadvantage—its comparatively infrequent but very serious toxic effect on the optic nerve.

In 1921 Sazerac and Levaditi introduced bismuth, which met with immediate acceptance and, to a very large extent, replaced mercury.

Fever Therapy

It had long been recognized that heat or fever will cure some diseases. Gabriel Fallope in "Tractatus de Morbo Gallico" (1560) forecast the use of the modern fever cabinet and gave illustrations of syphilitics undergoing mechanically induced fever therapy; Jeanselme in the "Histoire de la Syphilis" (1931) wrote a graphic account of the mediaeval method of producing fever. The patient was placed, either sitting or standing, in an enclosed chamber, with only his head exposed to the air. Below this was a brazier on to which were thrown from time to time a powder containing cinnebar or, better still, pastilles of terebinth or styrax (Figure). If the victim fainted he was revived by fresh air conducted through a long tube from the outside. Each treatment lasted from a quarter to one hour, after which the patient was put in a warm bed, covered with blankets, and left to continue the sweating process for a further hour. At the end of this period he was dried and given a glass of wine and something to eat. Six to nine treatments given every 2 or 3 days were recommended.

We are indebted to Breutsch (1946) for the translation of a manuscript for an unpublished monograph on "The History of the Malaria Treatment of General Paralysis" by Wagner-Jauregg. The rationale of malaria therapy was based on the observation that psychotics occasionally showed great improvement after an intercurrent feverish illness. In 1887 Wagner-Jauregg, while claiming no originality for his proposal, put forward the idea of intentionally inducing a febrile disease, suggesting malaria or erysipelas, as a therapeutic method. He selected the streptococcus of erysipelas as the lesser of the two risks but this proved entirely unsatisfactory. In 1890, with the appearance of



FIGURE—Medieval method of producing fever (Jeanselme, 1931).

Robert Koch's tuberculin, a new type of fever-producing agent became available, and Wagner-Jauregg began treating patients with this at the Psychiatric Clinic at Graz in Austria. At first he applied it to all types of mental patients but, after observing the unusual occurrence of apparent cure in a few cases of GPI, he concentrated his attention on this disease. After a 4-year trial of tuberculin injections alone, he combined these with mercury injections, because, as he said, "I never could convince myself that specific antisyphilitic treatment of general paralysis was without any value whatsoever, a view held by most psychiatrists of that period". Although with the combined tuberculin-mercury therapy complete remissions were obtained, relapses were frequent. In an attempt to improve on this, he tried various vaccines, finally selecting typhoid vaccine as the most reliable fever-producing agent, and replacing mercury by the recently introduced salvarsan. But still permanent remissions were few and relapses common. It was not till 30 years later, in 1917, that Wagner-Jauregg returned to his previous idea of malaria therapy. At that time infectious material was abundant in soldiers returning from the Balkan front: hospitals were

full of wounded personnel and by accident a minor casualty suffering from malaria had been admitted to one of Wagner-Jauregg's wards. An assistant physician asked: "Should he be given quinine?" "No", was Wagner-Jauregg's reply. "This I regarded as a sign of destiny, because soldiers with malaria were not usually admitted to my wards, which took only cases suffering from a psychosis or with injuries to the central nervous system." On that day (June 14, 1917) three general paralytic patients were inoculated by rubbing a few drops of the soldier's blood into several superficial scarifications of the skin. The favourable reports of his method of treatment were, at first, received sceptically by colleagues and other workers, but later clinicians in Vienna and elsewhere on the Continent hailed the new discovery and in 1927 Wagner-Jauregg was awarded the Nobel Prize for his work.

British psychiatry was conservative and reluctant to give this new treatment a trial, and it was not until July, 1922, that the first general paralytic was inoculated in Britain at Whittingham Mental Hospital by Dr. R. M. Clark with malaria supplied by Professor J. W. W. Stephens, F.R.S., who at that time occupied the Chair of Tropical Medicine

at Liverpool University. Cases continued to be infected somewhat sporadically during the next 3 years until on May 24, 1925, the Malaria Therapy Centre (now the Mott Clinic) was established at Horton Hospital, Epsom, from which infective material is supplied to hospitals all over the British Isles and as far afield as the Continent.

It has been my good fortune to be associated with this centre since its inception by the late Col. S. P. James, F.R.S., and Mr. P. G. Shute, who still continues his researches in malaria, parasitology, and entomology at Horton. The large numbers of general paralytics (now over 3,000) passing through this clinic have provided ample scope for research, and I should like to record the names of Drs. E. L. Hutton and M. Whelen who have worked with me over the past years, and also, for a limited period, the late Dr. Felix Plaut. Nor do we forget the encouragement and help we received from Prof. F. L. Golla, who succeeded the late Sir Frederick Mott at the Maudsley Hospital, and also Col. L. W. Harrison of St. Thomas' Hospital and the Ministry of Health.

The changed outlook on this hitherto fatal disease stimulated research throughout Europe and the United States with the production of a spate of literature. There were difficulties in the appraisal of this new therapeutic measure, because in most clinics it was supplemented by either trivalent or pentavalent arsenicals. At Horton, for the first 7 years, malaria alone was employed and trials of different species of malaria were made: benign tertian (*P. vivax*), quartan (*P. malariae*), malignant tertian (*P. falciparum*), and *P. ovale*.

The most commonly used species is benign tertian, though quartan is useful for the patient who has developed immunity to the former by residence in the tropics. It was at first thought that malignant tertian might produce better results with the predilection of this parasite to sporulate in the brain capillaries and other internal organs: however, it soon became apparent that no particular species of malaria was superior to any other as a therapeutic agent. The immediate results compared favourably with those at other clinics where malaria was supplemented with chemotherapy: life was prolonged, the physical condition of the patient was greatly improved, roughly one-third of the patients were discharged from mental hospitals, one-third, though hospitalized, had the disease process arrested at varying clinical levels, and in the remaining third gradual deterioration supervened.

The hazards of malaria and the expert management necessary led many workers to explore other means of producing fever. In America, and to a limited extent in Great Britain, inducto-therapy

and the Kettering hypertherm were employed. Hutton (1941), in a review of the aetiology and treatment of neurosyphilis, writes:

Although these methods are undoubtedly capable of exerting a curative effect on neurosyphilis, perhaps equal to that of malaria, it would seem that for the majority of cases they have no real advantages over malaria, which for general purposes is still the simplest and most easily administered form of therapy.

It is of interest to record that the advent of malaria therapy gave a great stimulus to the study of malariology. For the first time an opportunity had been given to study malarial infection as an experimentally produced condition: never before had it been possible to observe the clinical course of the disease in the primary attack. Much work was done on prophylaxis and testing out new synthetic antimalarial drugs. We may well claim that psychiatry has made a valuable contribution to another branch of medicine and that the discoveries have exercised far-reaching effects in the field and in the epidemiology of malaria.

Penicillin

Penicillin has been the means of the third advance in the treatment of syphilis in this century—1910 arsenic, 1917 malaria, 1943 penicillin—and has the unique characteristic of being efficacious at all stages of the disease and in all its manifestations. A vast literature has accrued which it is inappropriate, if not impossible, to review in a communication of this sort. There are, however, certain points in connexion with penicillin treatment of neurosyphilis which are worth consideration.

It is curious that the two most successful therapeutic agents in GPI—malaria and penicillin—should act in totally different ways. Although *T. pallidum* is susceptible to heat, neither Wagner-Jauregg nor many other later observers believed that the efficacy of malaria was entirely due to the temperature reaction. Wagner-Jauregg, from a theoretical viewpoint, reasoned that the fever could not be solely responsible, since improvement set in after the febrile period ended, and in a fair number of cases there was an exacerbation of symptoms during it. This view has received considerable support from the experimental observation that a body temperature from 106 to 110° F. is required to inhibit the syphilitic organism, and that temperatures between 103 and 105° F. have no significant effect (Frazier and Frieden, 1946). In addition, improvement in GPI cases who developed little or no fever has been reported by many clinical observers—Hermann, Wagner-Jauregg, Claude, Leroy, Médakovitch, Moore, Bahr, and Bruetsch—all quoted by Bruetsch (1949), who in a detailed study, maintains that the principal therapeutic factor is the activation

of the reticulo-endothelial system, leading to the production and stimulation of macrophages and the development of immune reactions, thereby inhibiting the treponemata. Hence the action of malaria is indirect and relatively slow. Penicillin, on the other hand, is a powerful spirochaeticidal agent and acts directly and relatively rapidly.

An apparent anomaly, which has since been explained, was the fact that units, such as the Mott Clinic, where aqueous penicillin was administered only once or at the most twice daily, obtained as good results as the more orthodox centres, where the round-the-clock method was employed. The explanation was provided by the laboratory workers, who showed that the important factor was not the continuous maintenance of a therapeutic blood-level, but the *time* required for the spirochaete to survive and reproduce. The drug must, therefore, be administered in such a way that there is no penicillin-free interval long enough for the surviving organisms to multiply. In the case of the *T. pallidum*, this all-important time interval is in the region of 30 hours, so that injections of penicillin once or twice in 24 hours are entirely adequate.

Since the advent of the penicillin treatment of neurosyphilis, the Herxheimer reaction, long familiar to the venereologist, has appeared in the field of the neurologist and psychiatrist. The figures of the incidence of the reaction are extremely variable and there seems to be no explanation forthcoming for the discrepancies. At the Mott Clinic we have been fortunate and our figures up to the present time have been extremely low. The usual explanation, that it is due to the sudden destruction of large numbers of spirochaetes and the subsequent liberation of breakdown products, does not appear to account for all the observed facts, and Heyman, Sheldon, and Evans (1952), in a detailed study, have put forward the hypothesis that the reaction is a delayed type of hypersensitivity phenomenon. The prevention of the Herxheimer reaction in neurosyphilis seems to be slightly more of a problem than it is in early syphilis. The use of a small initial dose of penicillin, which is gradually stepped up to the full therapeutic amount, is a useless procedure. A preliminary course of bismuth, a satisfactory prophylactic method in early syphilis, is not necessarily successful in neurosyphilis; in fact, Sinclair and Webster (1951) reported failure to prevent the reaction in five patients receiving heavy metal therapy right up to the beginning of penicillin treatment. There have been no reports of a Herxheimer reaction occurring where fever therapy has preceded penicillin administration; malaria has even been suggested as a prophylactic in this connexion!

Reports of severe and even fatal anaphylactic reactions to penicillin have been published. In view of this, the recommendation has been put forward that, before administration, patients should be investigated for the possibility of penicillin sensitivity, and, where this is found or is suspected, the drug should be withheld.

There is no doubt that the employment of penicillin is remarkably successful in the treatment of some cases. Many penicillin failures reported in the early days were probably due to inadequate dosage: the generally accepted view nowadays is that at least 10 mega units should be given.

It is always interesting and sometimes profitable to speculate. In 1946 Nicol analysed the results of a 10-year follow-up of two groups of 217 patients, treated respectively by malaria alone and malaria plus tryparsamide. He found decidedly better results, both clinically and serologically, in the combined-treatment group. The survival rates of the two series fully confirmed the superiority of malaria plus tryparsamide over malaria alone, since at the end of the 10-year period there were 20 per cent. fewer deaths among the patients who had received the combined treatment. The time is approaching when it will be possible to make a similar analysis of the results of a 10-year follow-up in two groups, treated respectively with penicillin alone and penicillin plus malaria.

In a personal communication, Sir Gordon Covell gave me the results of an investigation into the position of penicillin in the treatment of neurosyphilis which he had begun in 1954. A questionnaire, circulated to various centres throughout the United States and Europe, included the following questions:

- (1) What is the present trend in the incidence of neurosyphilis?
- (2) To what extent are (a) penicillin, (b) malaria therapy, being used for the treatment of neurosyphilis?
- (3) Are any figures available giving the proportion of cases treated with penicillin who have failed to respond to treatment or who have relapsed within a period of 2 years after treatment?
- (4) Do you know of any evidence suggesting that *T. pallidum* is becoming resistant to penicillin?
- (5) What is considered the treatment of choice for neurosyphilis?

The answers to questions (1) and (4) were unequivocal. It was the universal experience that the incidence of neurosyphilis, and especially GPI, had been steadily decreasing; and no evidence was forthcoming of the development of a penicillin-resistant strain of *T. pallidum*.

The replies to the other three questions were more indefinite. This may be an expression of the

fall in incidence of GPI, since the relative scarcity of cases would tend to make any assessment more difficult. One problem, however, is mentioned in the communications both from Canada and the United States: the difficulty of obtaining malaria for therapeutic purposes. In Canada the method of choice is penicillin plus malaria, although penicillin alone is largely used owing to the lack of available malaria; this is not usually considered sufficient and is often supplemented by tryparsamide. The replies from the United States vary—Bruetsch (Indianapolis) maintains that penicillin is probably adequate by itself; in Maryland and the Boston Psychopathic Institute malaria therapy is still used, but only in cases which have relapsed. On the other hand, Eldridge of the St. Elizabeth Hospital, Washington, thinks there is a decided risk of the ultimate development of a penicillin-resistant strain of *T. pallidum* and feels that penicillin alone is definitely inadequate.

In Europe the position seems to be somewhat different. There is a general consensus of opinion in Austria, Belgium, Czechoslovakia, France, Germany, Holland, Italy, Norway, Sweden, and Switzerland that the method of choice in GPI is combined treatment, that is, malaria plus penicillin. The remaining two countries from whom replies were received, Denmark and Russia, differ. In Denmark, patients are treated in the Kettinger hypertherm and given penicillin, unless they are in mental hospitals, when the treatment is penicillin alone. In Russia, it is thought that fever therapy is indicated only in cases resistant to penicillin.

The general trend towards the combined treatment of penicillin plus malaria, shown by the replies to the questionnaire, came as a considerable surprise, since, up to the present, there is no indication in the literature of this apparent change. Penicillin has largely usurped the role played by malaria, but my long experience of this disease leads me in the same direction: combined therapy is probably the method of choice, at any rate in parenchymatous neurosyphilis.

Long Term Follow-up

Serological.—In 1936 I visited the Wagner-Jauregg Clinic in Vienna and had the honour of being shown by Wagner-Jauregg himself the work that was being carried out. I was greatly impressed with the system of follow-up, and I well remember two taxi-drivers who had been treated some years previously driving up one Saturday afternoon to have their lumbar punctures done, and leaving the clinic immediately to ply their cars for hire in the streets of Vienna.

Though the serological follow-up was easy with in-patients, we had not adopted this procedure with out-patients. For some years a clinical follow-up at the Maudsley Hospital had been held, and I suggested to Professor Golla that we should do out-patient lumbar punctures, and received the rather discouraging reply that if I wanted to close down the clinic such a procedure would afford a good opportunity. However, by dint of persuasion and full explanation to the patients, a good start was made and the clinic still continues.

It is now universally accepted that repeated examination of the spinal fluid at 6-monthly intervals provides a useful guide in the evaluation of the therapy.

In a paper read before this Society in 1937, Nicol and Hutton stressed the effectiveness of malaria as a spirochaetocidal agent in about 85 per cent. of cases, as evidenced by the reversal of the serological findings after treatment: on the other hand, the number of genuine clinical recoveries was probably not much above 20 per cent. To explain this disappointing recovery rate they put forward the hypothesis that before the spirochaetes in the brain were killed, irreparable damage had already been done: in fact, the only indication for a further course of treatment was for those patients in whom the abnormalities in the spinal fluid remained obstinately positive, with the assumption that the spirochaetes were still active. Another important observation was the frequency with which the blood serum remains positive and the futility of trying to render it negative by further useless therapy.

In the U.S.A., Dattner, Carmichael, De Mello, and Thomas (1952) have stressed the importance of spinal fluid examination almost to the exclusion of considering the clinical condition of the patient, and criticism has been levelled at the concept of what is referred to as "treating the spinal fluid and not the patient". Nevertheless, the state of activity or inactivity of the spinal fluid is all-important and these workers put forward the plea that "the first goal of treatment must be complete elimination of the infective agent in the shortest possible time with the greatest safety to the patient". In the course of their studies two conclusions were reached:

(1) No significant clinical improvement can be expected from further antisyphilitic therapy in patients whose spinal fluid findings have indicated persistent inactivity of the syphilitic infection, further treatment of patients who continue to be psychotic must be directed against the psychosis and not against the *T. pallidum*;

(2) Relapses of neurosyphilis, including GPI, do not occur more than 2 years after treatment has produced spinal fluid findings which indicate an inactive process.

Wheien, in 1946, investigated some 872 patients, whose spinal fluid examinations extended from 1 to 15 years after treatment. Her conclusions were that the great majority of negative fluids become so within 3 years of the end of treatment, though the length of time varies considerably with individual patients. As stressed by Dattner, the most important finding in a fluid is the cell content, which is a reliable indicator of whether or not further treatment will be needed. Another conclusion arrived at, which is of immense practical importance, was that serial examinations of the cerebrospinal fluid should be made until at least two consecutive negative results had been obtained. In the light of subsequent experience we feel that this statement is perhaps a little optimistic and we are convinced that patients with syphilis of the central nervous system should remain under observation for life.

A good illustration of this was afforded by a 52-year-old messenger at Somerset House who was admitted to Horton Hospital in January, 1936, when he was grossly confused and emotionally unstable. The spinal fluid findings were strongly positive. Benign tertian malaria was given a month later, followed by a course of tryparsamide. He steadily improved and was discharged recovered in September of the same year. Two months later he returned to his former employment and remained in it for 17 years until his death. He attended the follow-up clinic regularly, but in spite of two consecutive negative fluid findings indicating inactivity, the fluid subsequently revealed abnormalities, which steadily increased until 1949 when it was a typical Group 3 fluid. All this time he remained clinically well. In May, 1951, he was given 15.6 mega units of Distaquine penicillin, with resultant improvement in the spinal fluid (Table). Unfortunately, he died in September, 1953, of cerebral haemorrhage following a fall at work.

BLOOD AND CEREbroSPINAL FLUID RESULTS
OF PATIENT

Date	Wassermann* Reaction	Cells	Protein	Lange
January 3, 1936	Str. +	61	50	5554310000
October 9, 1937	negative	—	30	0000000000
April 23, 1938	negative	—	20	0000000000
December 28, 1942	+ 3	2	30	0012232100
December 28, 1943	+ 3	3	Pandy*	1233210000
December 27, 1944	+ 6	—	30	—
February 20, 1946	+ 6	14	50	0122110000
March 4, 1946	+ 6	5	40	0122110000
February 23, 1947	+ 6	—	50	1223311000
February 9, 1948	+ 6	25	60	1223321000
March 6, 1949	+ 48	96	40	5543310000
April 30, 1950	+ 24	2	40	5555432100
March 18, 1951	+ 24	40	40	5554321000
May 11, 1952	+ 12	9	45	1110000000
August 23, 1953	Lumbar puncture failed			

*Blood, MKR and Kahn consistently positive.

Clinical.—The clinical results of treatment of GPI are of theoretical interest, ranging as they do from recovery with complete return to the pre-illness level, through a gradual descent to increasing

dementia, extending from the very mildest defect to profound deterioration.

Kral and Dörken (1953) carried out a comparative serological and psychological investigation on 52 institutionalized cases of dementia paralytica in the Verdun Protestant Hospital, Montreal. They found that the treated cases with negative spinal fluid showed a more pronounced deficit both of intelligence and of personality resources than those cases in an active phase. Clinically, this group of serologically negative cases can be subdivided into groups, one where apparently no further progress of the paralytic process occurs, and a second group where, despite a permanently negative fluid, a slow but definite deterioration can be recognized. To explain this, the authors maintain that their results indicate that at least two pathogenic factors are at work: one connected with the acute inflammatory process and responsible for the clinical picture and the fluid abnormalities, and relatively easily influenced by penicillin or combined therapy; and the other, long-acting, not influenced at all by therapy but responsible for progressive deterioration, even in the patient with a completely negative fluid. This second factor has been suggested by Merritt, Putnam, and Campbell (1937) to be of a vascular nature. This theory at any rate affords an explanation of those cases which in spite of therapy gradually deteriorate and in which the cause of ultimate death presents difficulties in evaluation, especially when intercurrent disease is not responsible.

In the Mott Clinic at Horton one of the most important aspects of the centre was the establishment of an adequate follow-up, which has now operated for 20 years. The personal contact between the clinic social services and the patient is one to be encouraged. This valuable work has been elaborated in recent years by Whelen and Bree (1946), who emphasized the importance of team work and the possibility of opening up "a great field of research, embracing mental hygiene, prophylaxis, and social medicine". They stressed the need for shifting the emphasis from the curing of the disease to the wider conception of the promotion of optimum health. The patient must be recognized as something unique; "a particular individual, in a particular family, in a particular environment". This means the inclusion of the patient's family and the enlistment of their help in retraining and rehabilitation.

In a more recent communication, Whelen and Bree (1954), investigated 132 cases of GPI and taboparesis, treated between 1942 and 1946, and subsequently discharged. Altogether, 39 of this group made a complete recovery, 81 exhibited

various degrees of improvement, eleven were stationary, and one could not be classified. All the recoveries took place within 3 years at the maximum. In the "improved" group of 81, only nineteen attained an optimal condition within three years, whereas 62 (78 per cent.) took longer. The patients who recovered did so, apparently, as the direct result of treatment, but in the improved group auxiliary factors, apart from adequate treatment, made an important contribution to their rehabilitation—a good pre-psychotic personality, a dependable and sympathetic prop (the family, friends, or even neighbours), and some kind of occupation, gainful or otherwise, that was within their capacity. The patients who came within the stationary group all lacked one or more of these factors.

These auxiliary factors are of great importance, not only in GPI, but in other forms of mental disorder as well, for example in post-leucotomy cases. Immense patience is needed; preventive social work of this nature may not be impressive, but it is more economical of the community's resources and returns some dividend in aiding those disabled people to some level of rehabilitation.

Discussion

In 1950 R. M. Stewart wrote:

No-one who is familiar with the vast literature devoted to neurosyphilis can fail to be impressed by the infrequency with which GPI now claims attention in current medical journals. The reason for this is not that man has become more continent or a less lascivious animal, but rather that new therapeutic advances have robbed syphilis of its more dangerous sequelae.

In the Chief Medical Officer's Annual Report to the Minister of Health for 1953, certified deaths from GPI were 91 men and 26 women; in 1911 to 1920 the average annual death rate was 1,697 men and 383 women. The "clinic" figures for neurosyphilis for the last 5 years show little change, but many of these cases are asymptomatic.

The *Journal of Venereal Diseases Information* ceased publication in December, 1951, and the *American Journal of Syphilis* in November, 1954, both for lack of material. The *British Journal of Venereal Diseases* remains the main English-speaking periodical dealing with these problems.

With the marked decrease of GPI one might well ask—why devote so much time to its study in a special centre like the Mott Clinic? But syphilis has not yet been eliminated and, until it has been, there will always remain that group of patients in whom the primary attack is so mild that it passes unnoticed, and those who, for one reason or another, have been inadequately treated. These people are always in danger of ultimately developing

late manifestations of syphilis, somatic or nervous. Nor must we neglect the very important problem of contacts: some are detected in routine examination, others at antenatal clinics, or in the investigation of families of patients suffering from GPI whether acquired or congenital. The incidence of venereal disease regularly rises during war, as the following figures from the late one show.

In 1946 infections of acquired syphilis rose to 10,705 men and 6,970 women: in 1939 the figures had been 3,574 and 1,412 respectively, not including service cases. If treatment for these primary attacks has been adequate, then late neuro-recurrences will not be seen; assuming that the average incubation period of general paralysis is 10 to 15 years, the next few years will give us the answer.

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